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THE IMPACT OF COVID-19 ON LOWER URINARY TRACT SYMPTOMS (LUTS) IN PATIENTS TREATED CONSERVATIVELY FOR BENIGN PROSTATIC HYPERPLASIA

Petar A. Antonov[1], Plamen K. Krastev[2]✉, Atanas S. Ivanov[1], Eleonora H. Hristova[3], Aleksander I. Timev[4]

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Abstract

Benign prostatic hyperplasia (BPH) is a non-malignant urological pathology characterized by a progressive increase in the volume of the prostate gland and one of the important diseases which affect lower urinary tract symptoms (LUTS). Covid-19 is a new viral infection with epidemiological characteristics of a pandemic. The disease is presented as a respiratory, cardiovascular, and neurological late complication. There is limited data that low urinary tract can be affected and aggravate symptoms and quality of life (QoL).

Our pilot study describes a male population treated with conservative methods for BPH and the effect of Covid-19 infection on their LUTS and QoL. This was a case-control study between April 2021 and November 2021. The study included 33 patients with a history of Covid-19 infection. The assessment of LUTS was carried out by processing the data obtained from the completed by the patients IPSS questionnaires (the last one before, immediately, and five months after Covid-19). The control group consisted of 50 patients, which for the management of the selection bias, matched according to demographic and clinical features of the group. All patients underwent ultrasound diagnostics giving information about the volume of the prostate gland and the amount of residual urine.

Two years after the beginning of the Covid-19 pandemic, we can confidently say that not all characteristics of this type of infection are sufficiently

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clear. More in-depth studies on Covid-19 as a cause of worsening LUTS and overall progression of BPH could help identify new aspects of infection leading to significant improvements in its treatment.

Key words: Covid-19, lower urinary tract symptoms, effects of Covid-19, Covid-19 and BPH

Introduction. Benign prostatic hyperplasia (BPH) is a non-malignant urological pathology characterized by a progressive increase in the volume of the prostate gland and, in most cases, is observed in elderly patients [1]. The clinical manifestation of this disease is associated with the appearance of the so-called lower urinary tract symptoms (LUTS). LUTS are stratified into three major groups: voiding symptoms, storage symptoms, and post-voiding symptoms [2]. The subjective assessment of these symptoms by the patient himself can be obtained by completing the so-called IPSS questionnaire, which includes seven questions about LUTS and one concerning the quality of life (QoL). According to the obtained result, patients can be divided into several groups: 'asymptomatic' (0 points), 'mildly symptomatic' (1–7 points), 'moderately symptomatic' (8–19 points), and 'severely symptomatic' (20–35 points) [3]. Covid-19 was discovered as a disease in late 2019 in Wuhan, China. It had become a pandemic within a year, affecting a significant number of the world's population and leading to hundreds of thousands of deaths and irreversible complications [4]. Late complications after a Covid-19 infection in most cases affect the respiratory, cardiovascular, and nervous systems [5]. Literature data show that the incidence of Covid-19 is significantly higher among the male population over 60 years [6]. Given this fact, it is logical to assume that the pandemic will affect a large proportion of older men with BPH. According to our reference, data on the influence of Covid-19 on patients suffering from BPH are extremely poor.

Our study aimed to present the effect of Covid-19 infection on lower urinary tract symptoms in patients receiving drug therapy α-blocker, 5α-reductase inhibitor or combination therapy) concerning BPH. We compared the COVID-19 patient group with BPH with the control group with only BPH patients.

Patients and methods. This was a case-control study between April 2021 and November 2021. The study included 33 patients with a history of Covid-19 infection. All of them were usually followed up for BPH in two outpatient practices.

The control group consisted of 50 patients, which for the management of the selection bias, matched according to demographic and clinical features of the case group [7].

The case and control group included patients treated with α-blocker, 5α-reductase inhibitor, or combination therapy. Excluding criteria were: previous surgical interventions for BPH, radiation therapy in the pelvis, pre-existing lower

urinary tract infection, a catheter placed during treatment, and treated in intensive care units.

The cohort demographics were documented. The assessment of LUTS was carried out by processing the data obtained from the completed patients' IPSS questionnaires (the last one before, immediately, and five months after Covid-19). All patients underwent ultrasound diagnostics giving information about the volume of the prostate gland and the amount of residual urine.

The statistical information was processed with SPSS Statistics v.26 and presented graphically with Microsoft Excel 2019. For all tests, a level of significance $p > 0.05$ was adopted. Descriptive statistics, nonparametric tests, t-test, ANOVA, and Bonferroni post-hoc test were used for statistical analysis.

Results. The case study recruited a total of 33 patients of mean age 66.4±1.2 years. The mean body mass index (BMI) was 26.1 ± 1.6 kg/m^2. More than 50% of the patients were treated for Covid-19 at home. According to conservative therapy for BPH, 15 patients ($51.5 \pm 8.7\%$) were on α-blockers, 9 ($21.2 \pm 7.1\%$) on 5α-reductase inhibitors, and 9 ($27.3 \pm 7.8\%$) on combined therapy. Prostate volume was estimated by ultrasonography with a mean value of 63.4 ± 3.1 cm^3. PSA levels were evaluated in all patients with a mean value of 4.23 ng/ml as a standard procedure.

The objective parameters for LUTS before and after Covid-19 are presented in Table 1.

T a b l e 1

Objective parameters for LUTS before Covid-19 vs. after Covid-19 (IPSS – International Prostate Symptom score, QoL – quality of life, RUV – residual urine volume)

Variable	Before COVID-19 treatment			After COVID-19 treatment			t	p
	n	Mean	Std error of mean	n	Mean	Std error of mean		
IPSS	33	7.8	0.6	33	15.5	0.8	12.47	0.000
Prostate volume	33	63.4	3.1	33	64.1	3.2	2.48	0.018
RUV	33	14.3	2.4	33	24.6	3.9	3.37	0.002
QoL	33	2.0	0.2	33	4.5	0.2	12.14	0.000

There was a significant increase in all parameters before Covid-19 compared with after Covid-19 ($p < 0.05$). A re-study was conducted after five months, comparing only the results of IPSS recently. A statistically significant difference between the three studied groups was observed. IPSS after 5 months of treatment was 11.7 ± 0.6, which is higher than IPSS before treatment 7.8 ± 0.6 (F = 2.71; $p = 0.024$) and lower than IPSS after treatment 15.5 ± 0.8 (F = 4.29; $p = 0.002$). Regarding the severity of LUTS, there was a significant increase in the moderately symptomatic cases after Covid-19. This resulted from decreasing in the mild

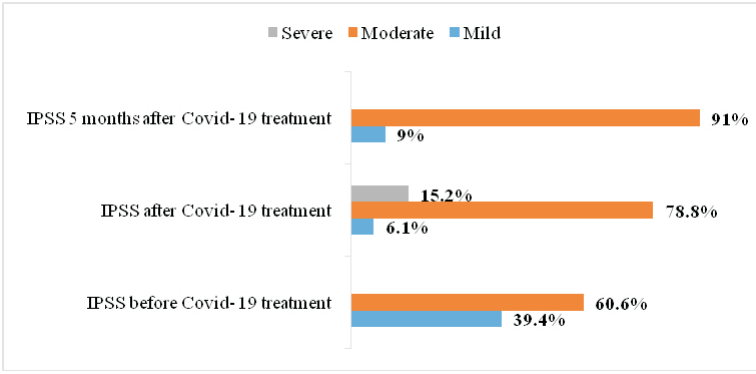

Fig. 1. The severity of LUTS before and after Covid-19 (IPSS – International Prostate Symptom Score)

symptom patients group, which was transformed to higher symptomatic groups – moderate and severe (Fig. 1).

There were no patients with complications as urine retention or urine incontinence. Deterioration of Quality of Life (QoL) was reported from 2.2 ± 0.2 before infection with Covid-19 to 4.5 ± 0.2 ($p < 0.05$).

Fifty patients were recruited for the control group with a mean age of 68.8 ± 0.9 years. The mean body mass index (BMI) was 26.9 ± 1.4 kg/m^2. There is not a statistical difference between IPSS before (9.6 ± 0.4) and IPSS after treatment (9.7 ± 0.4) and the Quality of Life ($2.08 \pm 0.1 \Rightarrow 2.04 \pm 0.1$) ($p > 0.05$). Prostate volume was estimated by ultrasonography with a mean value of 69.8 ± 1.5 cm^3 and increased after treatment to 70.6 ± 1.6 cm^3 ($p > 0.05$).

There is statistical difference between objective parameters for LUTS for case and control groups (IPSS – $t = 6.99$; $p = 0.000$ and QoL – $t = 10.45$; $p = 0.000$) (Fig. 2).

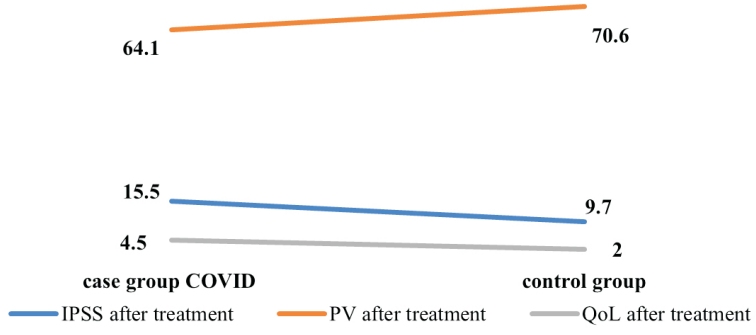

Fig. 2. Objective parameters for LUTS for case and control groups (IPSS – International Prostate Symptom score, QoL – quality of life, PV – prostate volume)

Discussion. According to the International Continence Society, LUTS is a concept that encompasses several symptoms related to the storage of urine, the act of urination, and the period after urination [2]. LUTS assessment is done by questionnaires such as the IPSS or the American Urology Association symptom score [8]. One of the most common causes of clinical manifestation of LUTS is BPH, especially in older men. Age is a significant risk factor in BPH development [9].

At the end of 2019, Chinese scientists isolated the new Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) by genomic sequencing. Shortly afterward, on January 12th, the World Health Organization (WHO) published its first report on it, and on March 11th, it declared a world pandemic of Covid-19 [10]. The most common clinical symptoms of Covid-19 are related to the respiratory system – fever, cough, and dyspnea. Some studies provide information on the urinary system and LUTS manifestation [11]. Several studies have shown that Covid-19 infection is characterized by a significantly higher incidence of complications and mortality in the male population. Hypotheses for the so-called sex-dependent (androgenic) immune response are also put forward [12].

According to our data, the research on the effects of Covid-19 on patients treated with BPH is very limited worldwide. The data that the virus uses urine as a pathway for transmission is only hypothetical, but there are studies with results that SARS-Cov-2 virus is possible to be excreted by urine [11]. Our research data showed that LUTS significantly increased in BPH conservatively treated patients suffering from Covid-19. There are two main options for medical treatment of BPH: 5-alfa reductase inhibitors (5ARIs) and Alpha-adrenoreceptor blockers (ARBs). Due to different action models, the combination of two groups is widely used. ARBs are the first-line therapeutic option because of their rapid mechanism of action, good efficacy, and low rate and severity of adverse events. Patients treated by ARBs are a more significant part [13]. In the literature, there is the suggestion that 5ARIs are more protectable for LUTS in male patients because they affect the androgen pathway on the one hand, and the hypothesis for an androgenic immune response on the other. We also report significant increase in RUV after COVID-19, but no patients have acute urine retention or urine incontinence. Summarizing all of the above statistical variables was the quality of life (QoL) data, which worsened after infection. QoL questions are an excellent additional clinical instrument by which we receive information for the effects of the disease in different people. Covid-19 decreases QoL in various ways – fear of death, changes in body function after hypoxia, and affecting normal physiology with another mechanism. After three months, parameters related to the quality of life were normalized [14]. Our results show that the prostate volume parameter was not statistically changed, but IPSS (15.5 vs. 9.7) in the case and control group and QoL (4.5 vs. 2) in the same groups changed dramatically.

According to our data, this study is one of the pilot ones regarding the relationship between Covid-19 and BPH-related LUTS. Our study also has some limitations – the small number of patients included, the lack of a control group, and the short follow-up period. Despite these limitations, we strongly believe that, as one of the few such studies, we would contribute to the growth of information on Covid-19 and its relationship to diseases of the genitourinary system.

Conclusion. Two years after the beginning of the Covid-19 pandemic, we can confidently say that not all characteristics of this type of infection are sufficiently clear. More in-depth studies on Covid-19 as a cause of worsening LUTS and overall progression of BPH could help identify new aspects of infection leading to significant improvements in its treatment.

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[1]*Department of Urology and General Medicine, Medical University of Plovdiv, 15A Vassil Aprilov Blvd, 4002 Plovdiv, Bulgaria*
e-mails: p_antonov@abv.bg,
atanasivanovmd@yahoo.com/atanas.ivanov@mu-plovdiv.bg

[2]*Cardiology clinic, St. Ekaterina University Hospital, 52A P. Slaveykov Blvd, 1431 Sofia, Bulgaria*
e-mail: plamenkr@mail.bg

[3]*Department of Social Medicine and Public Health, Faculty of Public Health, Medical University of Plovdiv, 15A Vassil Aprilov Blvd, 4002 Plovdiv, Bulgaria*
e-mail: eleonora.hristovaa@gmail.com

[4]*Department of Urology, Faculty of Medicine, Medical University – Sofia, 1 Georgi Sofiiski St, 1431 Sofia, Bulgaria*
e-mail: a.timev@gmail.com